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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
ANGELL, JON E

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/445,375	KINGSMAN ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *40,42,43,45,46 and 54-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-16,18-21,24,25,27-29,31-34,36-38,47-53,57,58 and 60-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4)☐ Interview Summary (PTO-413) Paper No(s) _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other.

DETAILED ACTION

Claims 1-10, 12-16, 18-21, 24, 25, 27-29, 31-34, 36-38, 40, 42, 43, 45-58, and 60-74 are pending in the application.

Claims 40, 42, 43, 45, 46, and 54-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claims 1-10, 12-16, 18-21, 24, 25, 27-29, 31-34, 36-38, 47-53 and 57-74 are examined herein.

Drawings

1. The drawings are objected to by the Draftsperson under 37 CFR 1.184 or 1.152 for the reasons indicated on attached form PTO 948.

2. Applicant is required to submit a proposed drawing correction **in reply to this Office action**. Failure to timely submit the proposed drawing correction will result in the abandonment of the application.

Double Patenting

Applicant was advised that should claim 58 be found allowable, claim 59 will be objected to under 37 CFR 1.75 as being a duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 58 and 59 are identical claims.

Claim Rejections - 35 USC § 102

1. The rejection of claims 1, 2, 3, 5, 6, 7, 8, 9, 10, 13, 14, 15, 17, 18, 19, 20, 21, 27, 28, 29, 31, 32, 34, 37, 38, 40, 49, 50, 51, 52, 53, 57, 58, 59 and 60 under 35 U.S.C. 102(b) as being anticipated by Stringer (WO 96/15238) have been considered but are moot in view of the amendment to the claims and the new ground(s) of rejection..

2. The rejection of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 15, 16, 20, 24, 27, 28, 29, 31, 32, 34, 47, 49, 50, 51, 52, 53, 57, 58, 59 and 60 under 35 U.S.C. 102(e) as being anticipated by Wickham et al. (US Patent number: 5,559,099, 1996) have been considered but are moot in view of the amendment to the claims and the new ground(s) of rejection..

3. Applicant's arguments with respect to claim 59 have been considered but are moot in view of the cancellation of claim 59.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 20, 21, 24, 25, 27, 28, 29, 33, 34, 38, 49, 50, 51, 52, 53, 58, and 59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to vectors and methods for delivering the vectors cancerous cells wherein the vectors are comprised of a polynucleotide or polynucleotides, as well as to

methods of treating or ameliorating cancer. Methods of targeting nucleic acids into an organism fall in to the broad category of gene therapy. While delivery of nucleic acids in and of itself is not considered a therapy per se, delivery shares many of the obstacles recognized for many of the actual therapy methods because successful therapy methods are for the most part, based on the ability to deliver exogenous nucleic acids to cells or tissues of interest. Thus, the rejection as a whole is appropriate for the claimed invention regardless of the embodiment (delivery vs. treatment) envisaged.

At the time of filing, the relevant art considered gene therapy as a whole to be unpredictable as modes of delivery that would provide efficient delivery and expression of genes encoding the protein in the target cells had not been fully developed. Clinical efficacy has not been achieved in any gene therapy protocol to date. The art is plagued by unpredictability. Regarding gene delivery and gene therapy, Anderson (Nature, April 30, 1998) teaches that, "[g]ene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease." Anderson (1998) also states, "[s]everal major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered", and " [t]he reason for the low efficiency of gene transfer and expression in human patients is that we still lack a basic understanding of how vectors should be constructed, what regulatory sequences are appropriate for which cell types, how *in vivo* immune defences (sic) can be overcome, and how to manufacture efficiently the vectors that we do make" (see page 30 under Conclusion). Furthermore, Verma et al (1997) teaches, "[t]here is still no single outcome that we can point to as a success story" (see Gene Therapy Promises, Problems and Prospects, Nature, Vol. 389, pg. 239, col. 1). Walther and

Stein (2000) indicate that the majority of clinical trials using viral vectors for gene therapy in humans still lack a significant clinical success, defining the still existing barriers to achieving clinical benefits with gene therapy (see pg. 267, discussion column). Mountain (2000) teaches that, "each gene transfer system has its own combination of advantages and limitations" (See Gene Therapy: the first decade, col. 5, pg. 121).

The claims are not enabled because the specification merely discloses instructions of how to construct vectors, and prophetic examples of how the vectors may be delivered to tumors and possible animal models that may prove to be useful in evaluating the efficacy of the proposed treatment. The specification does not disclose any evidence that the vectors actually deliver the polynucleotide(s) to the tumor, as required by the claims, or that the methods are effective at treating or ameliorating cancer. Such a disclosure is required in light of the relevant art that teaches the efficacy of gene therapy is unpredictable.

Thus to overcome the teachings in the art, the specification would need to supply direct, correlative guidance as to how to effectively administer the polynucleotides of interest. Also, required is evidence that the methods are effective at treating or ameliorating cancer. Without such guidance in the specification and lack of correlative working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan.

In conclusion, given the nature of the invention, the level of predictability, the amount of guidance set forth in the specification, and the working examples set forth, it is concluded that one of skill in the art would need to perform a vast amount of experimentation in order to

practice the invention commensurate in scope with the claims and this amount of experimentation is in fact undue.

Response to Arguments

6. Applicant's arguments with respect to claim 59 have been considered but are moot in view of the cancellation of claim 59.

7. Applicant's arguments filed 4/30/02 (Paper No. 19) regarding the rejection of claims under 35 U.S.C. 112, first paragraph, have been fully considered but they are not persuasive.

8. Applicants contend that is sufficiently described and exemplified in the specification to enable a person of ordinary skill in the art to carry out the invention. Applicants point out that the specification gives extensive guidance on the preparation of vectors of the invention and their uses in methods of gene delivery which may be used for treatment of disease such as cancer. Applicants also argue that examples are presented demonstrating delivery to animal models (Examples 4 and 9), and assert that guidance is given as to the assessment of efficacy to the macrophage and *in vivo* treatments (Examples 3, 4, 7, 8, and 9). Furthermore, Applicants have provided a declaration of one of the inventors, Dr. Miles Carroll, which demonstrates;

a) Intratumoral delivery of adenoviral vectors encoding scFv proteins specific to 5T4, and expression therefrom in mice;

b) Specific expression of B7-scFv in the sera of Balb/c mice;

c) Expression of a B7-scFv in a tumor following intratumoral delivery using the AdB7-scFv vector in mice;

d) The scFv-Hγ1 fusion protein is able to direct cytotoxicity against cells expressing the 5T4 antigen at the cell surface, wherein the targeted cells are *in vitro*;

e) The genetic delivery of a construct encoding the scFv- Hγ1 fusion protein using the MLV-LscFV Hγ1 to cancer cells leads to secretion of the protein from the cells and their binding back to the cell surface, wherein the cells are *in vitro*.

In response, it is acknowledged that Applicants have disclosed different vectors that may be used in the present invention for the treatment of diseases such as cancer. However, the specification only prophetically discloses examples of in vivo delivery to animals. Applicant's declaration provides evidence that an adenoviral vector can be delivered to a tumor in an animal only by intra-tumoral delivery (i.e. direct injection into the tumor). The evidence does not show that delivery of the vector of has any therapeutic effect on the tumors *in vivo*.

It is pointed out that the instant claims are drawn to methods of treatment and were rejected because the claims are not enabled for methods of treatment. Several factors were considered in determining whether the disclosure required undue experimentation (as mentioned in the previous Office Action and above). Among the factors that were considered was the unpredictability of the prior art. As mentioned above delivery is only one element of gene therapy that is unpredictable, others include sufficient expression of the therapeutic molecule for a sufficient amount of time to have therapeutic benefit, the response of the host's immune system to the treatment, and the fact the results in animal models have not been borne out in human trials (see Crystal p. 409, first column).

Therefore, although Applicants have shown that one particular vector can be delivered to a tumor only by intra-tumoral delivery, and that a vector can have a cytotoxic effect on cells *in vitro*. There is no evidence presented to overcome the unpredictability of gene therapy as recognized in the art because no evidence has been presented demonstrating administration of the claimed invention (vector) to a tumor *in vivo* such that delivery of the claimed vector results in the successful treatment of cancer *in vivo*. Therefore, the rejection of claims drawn to treatment of disease under 35 U.S.C. 112, first paragraph is maintained.

New Rejections

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-10, 12-16, 18-21, 24, 25, 36-38, 47-50, and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 1 recites the limitation "the tumor" in line 3. There is insufficient antecedent basis for this limitation in the claim. Dependent claims 2-10, 12-16, 18-21, 24, 25, 36-38, 47-50, and 60 are rejected for the same reason.

Claim Rejections - 35 USC § 103

12. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-10, 12-16, 18, 20, 27, 34, 36, 37, 47-49, 51, 57, 60-65, 71 and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (WO 96/30504) in view of Myers et al. (JBC Vol. 269, No. 12: p. 9319-9324; 1994).

Anderson teaches a retroviral vector comprising a polynucleotide encoding a tumor-interacting protein wherein the tumor interacting protein is targeted (i.e. binds) to a specific tumor cell type, and delivers a second polynucleotide of interest (e.g. a therapeutic product) to the interior of the tumor cell (e.g., see abstract; p. 1, paragraphs 1-2; p. 19, second paragraph; and paragraph bridging p. 20-21); wherein the vector delivers a second polynucleotide of interest which is a therapeutic polynucleotide (p. 21, second paragraph); wherein the polynucleotide comprises at least one tumor binding domain (i.e. a tumor binding protein, such as an antibody or part of an antibody) which binds with a tumor cell-associated surface molecule that is expressed on one cell type (here an antibody to erb-2, known in the are to be expressed on breast tumor cells; see paragraph bridging p. 7-8); and wherein the vector can be used for *in vivo* delivery of polynucleotide/product of interest (e.g. p. 2, second paragraph).

Anderson also teaches that the tumor interacting protein can be expressed as a fusion protein to a product of interest (here, the targeting polypeptide expressed as a fusion protein with specific envelope proteins, such as SEQ ID NOS: 1-5 (e.g., see last paragraph, p.3 through first paragraph, p. 7); and that the envelope proteins includes a secretory signal or "leader" sequence, thus making the fusion protein a secretory protein (i.e. secreted) (see paragraph bridging p. 6-7).

Anderson does not specifically teach a vector that binds to a trophoblast cell surface antigen, or that the trophoblast cell surface antigen to which the vector binds is 5T4.

Myers teaches the isolation of a cDNA encoding 5T4 Oncofetal Trophoblast Glycoprotein, and indicates that 5T4 (identified by a monoclonal antibody) has been shown to be "strongly expressed on fetal trophoblast membranes, but absent from most normal non-pregnant tissues with a few epithelia [being] weakly positive" and "is expressed by a wide variety of transformed embryonic and carcinoma-derived cell lines and many different human carcinomas." (See p. 9319, paragraph bridging columns 1 and 2), and can be used to target therapeutic molecules to several types of solid tumors, as evidenced by Forsberg et al. (JBC, Vol. 272 No. 19: 12430-12436; 1997).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make the vector taught by Anderson with a substituted tumor interacting protein, wherein the substituted tumor interacting protein is the antibody (or part thereof) that specifically interacts with 5T4 taught by Myers, to create the vector of the instant claims with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Anderson, who teaches "retroviruses can be made 'targetable' to a specific type of cell if a

portion of the receptor binding region is modified such that the receptor binding region includes a polypeptide which binds to a ligand or receptor of a target cell" and mentions many different specific examples (see middle of p. 7 through the end of p. 8) including "antibodies and fragments thereof, including single chain antibodies" (see paragraph bridging p. 7-8).

15. Claims 19, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (WO 96/30504) in view of Myers et al. (JBC Vol. 269, No. 12: p. 9319-9324; 1994) and further in view of Barber (U.S Patent 5,591,692; 1997).

Anderson teaches a retroviral vector comprising a polynucleotide encoding a tumor-interacting protein wherein the tumor interacting protein is targeted (i.e. binds) to a specific tumor cell type, and delivers a second polynucleotide of interest (e.g. a therapeutic product) to the interior of the tumor cell (e.g., see abstract; p. 1, paragraphs 1-2; p. 19, second paragraph; and paragraph bridging p. 20-21); wherein the vector delivers a second polynucleotide of interest which is a therapeutic polynucleotide (p. 21, second paragraph); wherein the polynucleotide comprises at least one tumor binding domain (i.e. a tumor binding protein, such as an antibody or part of an antibody) which binds with a tumor cell-associated surface molecule that is expressed on one cell type (here an antibody to erb-2, known in the are to be expressed on breast tumor cells; see paragraph bridging p. 7-8); and wherein the vector can be used for *in vivo* delivery of polynucleotide/product of interest (e.g. p. 2, second paragraph).

Anderson also teaches that the tumor interacting protein can be expressed as a fusion protein to a product of interest (here, the targeting polypeptide expressed as a fusion protein with specific envelope proteins, such as SEQ ID NOS: 1-5 (e.g., see last paragraph, p.3 through first

paragraph, p. 7); and that the envelope proteins includes a secretory signal or "leader" sequence, thus making the fusion protein a secretory protein (i.e. secreted) (see paragraph bridging p. 6-7).

Anderson does not specifically teach a vector that binds to a trophoblast cell surface antigen, or that the trophoblast cell surface antigen to which the vector binds is 5T4.

Myers teaches the isolation of a cDNA encoding 5T4 Oncofetal Trophoblast Glycoprotein, and indicates that 5T4 (identified by a monoclonal antibody) has been shown to be "strongly expressed on fetal trophoblast membranes, but absent from most normal non-pregnant tissues with a few epithelia [being] weakly positive" and "is expressed by a wide variety of transformed embryonic and carcinoma-derived cell lines and many different human carcinomas." (See p. 9319, paragraph bridging columns 1 and 2), and can be used to target therapeutic molecules to several types of solid tumors, as evidenced by Forsberg et al. (JBC, Vol. 272 No. 19: 12430-12436; 1997).

Neither Anderson nor Myers teaches that the retroviral vector further comprises tumor specific promoter.

Barber teaches a recombinant retroviral vector which can be targeted to preselected cell lines and wherein the vector comprises tissue-specific promoters such as tumor-specific promoters (e.g., transferring receptor or Thymidine kinase; see column 4, lines 1-10 and column 21, line 12 through column 22 line 21).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Anderson and Myers (as mentioned above) with the teachings of Barber to create the vector of the instant claims with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Anderson, who teaches the retroviral vector may further comprise a sequence encoding a therapeutic agent under the control of a suitable promoter (see paragraph bridging pages 13 and 14 and p. 15, second paragraph), and can be used to treat tumors (see paragraph bridging p. 20-21), thus indicating that expression of the therapeutic agent in tumor cells would be desirable.

16. Claim 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (WO 96/30504) in view of Myers et al. (JBC Vol. 269, No. 12: p. 9319-9324; 1994) and (U.S Patent 5,591,692; Jan. 7, 1997) and further in view of Willis (EP 0 803 574 A2; 1997).

Anderson teaches a retroviral vector comprising a polynucleotide encoding a tumor-interacting protein wherein the tumor interacting protein is targeted (i.e. binds) to a specific tumor cell type, and delivers a second polynucleotide of interest (e.g. a therapeutic product) to the interior of the tumor cell (e.g., see abstract; p. 1, paragraphs 1-2; p. 19, second paragraph; and paragraph bridging p. 20-21); wherein the vector delivers a second polynucleotide of interest which is a therapeutic polynucleotide (p. 21, second paragraph); wherein the polynucleotide comprises at least one tumor binding domain (i.e. a tumor binding protein, such as an antibody or part of an antibody) which binds with a tumor cell-associated surface molecule that is expressed on one cell type (here an antibody to erb-2, known in the are to be expressed on breast tumor cells; see paragraph bridging p. 7-8); and wherein the vector can be used for *in vivo* delivery of polynucleotide/product of interest (e.g. p. 2, second paragraph).

Anderson also teaches that the tumor interacting protein can be expressed as a fusion protein to a product of interest (here, the targeting polypeptide expressed as a fusion protein with specific envelope proteins, such as SEQ ID NOS: 1-5 (e.g., see last paragraph, p.3 through first paragraph, p. 7); and that the envelope proteins includes a secretory signal or "leader" sequence, thus making the fusion protein a secretory protein (i.e. secreted) (see paragraph bridging p. 6-7).

Anderson does not specifically teach a vector that binds to a trophoblast cell surface antigen, or that the trophoblast cell surface antigen to which the vector binds is 5T4.

Myers teaches the isolation of a cDNA encoding 5T4 Oncofetal Trophoblast Glycoprotein, and indicates that 5T4 (identified by a monoclonal antibody) has been shown to be "strongly expressed on fetal trophoblast membranes, but absent from most normal non-pregnant tissues with a few epithelia [being] weakly positive" and "is expressed by a wide variety of transformed embryonic and carcinoma-derived cell lines and many different human carcinomas." (See p. 9319, paragraph bridging columns 1 and 2), and can be used to target therapeutic molecules to several types of solid tumors, as evidenced by Forsberg et al. (JBC, Vol. 272 No. 19: 12430-12436; 1997).

Neither Anderson nor Myers teaches that the retroviral vector further comprises tumor specific promoter.

Barber teaches a recombinant retroviral vector which can be targeted to preselected cell lines and wherein the vector comprises tissue-specific promoters such as tumor-specific promoters (e.g., transferring receptor or Thymidine kinase; see column 4, lines 1-10 and column 21, line 12 through column 22 line 21).

Anderson, Myers and Barber do not teach that the tumor interacting protein is operably linked to a tumor-specific expression regulatory element, or that said tumor interacting protein further comprises an effector domain such as all or part of a cytokine, a toxin, pro-drug activating enzyme, or enzyme.

Willis teaches a retroviral vector which produces a fusion protein which comprises a modified gag gene fused to a heterologous gene (see abstract); wherein the heterologous gene can encode cytokines or other therapeutic proteins (column 7, lines 40-50) or proteins which need to be targeted to a specific cell for therapeutic purposes (see column 7, lines 53-56).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Anderson, Myers and Barber (as mentioned above) with Willis to create the vector of the instant claims with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by both Willis and Anderson. Willis indicates that the fusion protein can be useful for proteins which need to be targeted to a specific cell for therapeutic purposes (see column 7, lines 54-56). Anderson indicates who teaches the vector may be used for delivering a therapeutic agent to a to a tumor for treatment (see paragraph bridging p. 20-21), thus indicating that expression of the therapeutic agent (such as the fusion protein comprising 5T4 (suggested by Anderson and Myers) and a therapeutic agent, such as a cytokine (as suggested by Willis) in tumor cells would be desirable.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J Eric Angell
July 15, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER

Continuation of Disposition of Claims: Claims pending in the application are 1-10,12-16,18-21,24,25,27-29,31-34,36-38,40,42,43,45-58 and 60-74.